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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,945	06/21/2002	Gerald H Thomsen	10624-092	8725
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Pennie & Edmonds 1155 Avenue of Americas New York, NY 10036-2711			EXAMINER ROBINSON, HOPE A	
			ART UNIT 1653	PAPER NUMBER

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/009,945

**Applicant(s)**

THOMSEN ET AL.

**Examiner**

Hope A. Robinson

**Art Unit**

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 37-80 is/are pending in the application.
- 4a) Of the above claim(s) 37-68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 69 and 75-80 is/are rejected.
- 7) ☒ Claim(s) 70-72 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 December 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 1/10/03.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Application Status***

1. Applicant's election with traverse of Group IX (claims 69-72) on July 1, 2004 is acknowledged.
2. The traversal is on the ground(s) that Group I (claims 37-40, 61 and 65), Group II (claims 41-44) and Group IX (claims 69-72 and new claims 75-80) should be rejoined and examined together. It is stated that Groups I, II and IX each relate to Smurf polypeptides. It is further stated that a search for the subject matter of Group IX should uncover any relevant art pertaining to the Smurf polypeptides of Group I and II, thus applicants assert that to search and examine the claims of Groups I, II and IX would not be a serious burden on the Examiner. MPEP 803 is cited and applicant request that the Restriction Requirement under 35 U.S.C. 121 be modified such that the subject matter of Groups I, II and IX are examined together in the same application. Applicants also state that the reference cited by Beach et al. (WO 97/12962) does not teach SEQ ID NO:2.

Applicant's arguments have been considered and are partially persuasive. First, applicant's statement that the Restriction Requirement under 35 U.S.C. 121 is improper based on MPEP 803, is incorrect. This argument is not germane to Lack of Unity practice under 35 U.S.C. 121 and 372. The present application is a 371 (national stage) of PCT/US 001/16250, as such the application is subject to a Lack of Unity, for which

the criteria is "unity of invention and special technical feature", burdensome search is not a criteria. Therefore, applicant's comments regarding MPEP 803 and search burden are noted but will not be further commented on.

Secondly, the inventions present in the instant application lack a special technical feature as the invention of for example Group I does not escape the prior art (see Beach et al., WO 97/12962, April 10, 1997). It is noted that applicant argues that the cited reference does not teach SEQ ID NO:2, however, this argument is not persuasive. Group I is directed to "a Smurf polypeptide comprising greater than 70% homology with an amino acid sequence depicted in SEQ ID NO:2" (see for example claim 37). Beach et al. teach a sequence that is 77.3% identical to SEQ ID NO:2 of the instant application. In addition, Beach et al. teach a sequence that is 99.8% identical to the claimed sequence set forth in SEQ ID NO:4 (alignment attached). Thus, the present application lacks a special technical feature as the claimed polypeptide does not avoid the prior art.

Upon due reconsideration applicant's request for a rejoinder of Groups I and II has been granted as SEQ ID NO:2 and 4 have some overlap, however, Groups I-II and IX will not be rejoined, thus applicant's arguments were partially persuasive. Note that based on the rejoinder of Groups I and II, the claimed inventions have been regrouped as follows and the elected group is now Group VI. This response is deemed sufficient to address applicant's arguments. Therefore, based on PCT Rule 13.1 the Lack of Unity of record has been maintained and is final.

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Group I, claim(s) 37-44 and 65 are drawn to an Smurf polypeptide.

Group II, claim(s) 45-62 are drawn to a nucleic acid.

Group III, claim(s) 63-64 are drawn to a transgenic non-human animal.

Group IV, claim(s) 66 and 68 are drawn to a method for promoting a bone morphogenic protein or tumor growth factor-beta activation pathway.

Group V, claim(s) 67 is drawn to a method for inhibiting a bone morphogenic protein.

Group VI, claim(s) 69-72 and 75-80 are drawn to a method of screening for a modulator of Smurf activity.

Group VII, claim(s) 73-74 are drawn to an antibody that binds the amino acid.

3. Claims 1-36 have been cancelled. Claims 75-80 have been added. Claims 37-80 are pending. Claims 69-72 and 75-80 are under examination. Claims 37-68 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

4. The Preliminary Amendment filed on July 9, 2003 has been received and entered.

### ***Specification***

5. The specification is objected to because of the following informalities:



JON WEBER  
SUPERVISORY PATENT EXAMINER

(a) The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademarks such as FLAGS<sup>TM</sup>, TRIS®, for example, have been noted in this application (see page 47). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

(b) The specification is also objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see for example page 22, line 4. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

(c) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "MODULATORS OF SMURF AND ANTAGONISTS OF BMP/TGFBETA SIGNALING PATHWAYS". See MPEP § 606.01 regarding change in title.

Correction of the above is required.

### ***Drawing***

6. The drawings filed on December 11, 2001 are objected to because some of the figures are blurry, see for example Figure 2. In addition, the Brief Description of the drawing on pages 5-13 of the instant specification, is not accurate. Note that Figure 1

as displayed has parts A-D, however, the description on page 5 does not describe parts A-D. On page 7, Figure 5D is missing from line 31. On page 9, Figure 9 does not describe parts A-F; Figure 10 does not describe parts A-C and Figure 11 does not describe parts A-H. On page 11, Figure 17 does not describe parts C1-C4.

Correction of the above and the filing of formal drawings is required.

### ***Information Disclosure Statement***

7. It is noted that applicant filed an Information Disclosure Statement on January 10, 2003 and indicated that a copy of 90 publications were enclosed, however the non-patented references are missing from the application and cannot be considered at this time. The patented references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 76-77 and 79-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to Smurf activity of a Smurf comprising greater than 70% or 90% homology with the amino acid sequence depicted in SEQ ID NO:2 and a Smurf activity of Smurf comprising greater than 70% or 90% homology with the amino acid sequence depicted in SEQ ID NO:4. The instant specification on page 21 disclose that the term "homologous" refers to the relationship between proteins that possess a common evolutionary origin. It is also disclosed that "substantially homologous" is when greater than 70% of the amino acids are identical or greater than 90%. However, the instant specification does not provide adequate description of the genus of polypeptides encompassed in the claims. There is no indicia as to conserved regions of for example SEQ ID NOS: 2 and 4 or where in the sequences the modifications will occur. The instant specification does not adequately describe variants of the claimed sequences by structure or any characteristics to indicate possession of the claimed variants. Further, the claims do not recite any functional limitation to indicate that once modified the protein will retain the Smurf activity. Therefore, the skilled artisan cannot envision the detailed chemical structure of the polypeptides, thus, claims reciting % homology of the claimed sequences lacks adequate written description.

The genus of polypeptides encompassed in the claims is highly variable. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative



number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

The claimed genus of polypeptides could include non-functional proteins or proteins with a different function than the one described. Therefore, the genus of claimed polypeptides encompasses widely variant species. As such, neither the description of the structure and function of SEQ ID NOS: 2 or 4, for example "70% homology to SEQ ID NO:2 ", is sufficient to be representative of the attributes and features of the entire genus. Based on the unlimited variations contemplated one skilled in the art would at best expect a protein that is different or at worst a protein that is not functional.

*Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See Vas-

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*Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993).

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 69, 75-76 and 78-80 are rejected under 35 U.S.C 102(b) as being anticipated by Beach et al. (WO 97/12962, April 10, 1997) based the broad recitation of modulation of Smurf activity, the activity of the specific sequences, the broad recitation of "homology" and the disclosure that Smurf is E3 ubiquitin ligase (pages 5 and 13).

Beach et al. teach ubiquitin ligases, for example E3 ubiquitin ligase that is said to reduce ubiquitination, an art recognized activity of Smurf. Beach et al. teach a method for identifying an activator or an inhibitor of ubiquitin-mediated proteolysis of a cell-cycle regulatory protein...measuring the level of ubiquitination of the subject protein brought about by the system in the presence and absence of a candidate agent (page 8). Beach et al. also teach competitive binding assay to detect potential modulatory agents in the presence and absence of a test agent for the ubiquitin pathway ( page 9 of the reference), which anticipates the screening method of claim 69. The reference also anticipates the claimed invention of claim 75, as the claim merely requires the activity of the sequence not the sequence *per se*, and the reference teaches a sequence that is 77.3% identical to SEQ ID NO:2 (claim 76) having a E3 ubiquitin ligase activity (Smurf), see the attached alignment. Beach et al. teach a sequence that is 99.8% identical to the sequence set forth in SEQ ID NO:4, thus anticipates claims 79-80. Beach et al. also anticipates claim 78 because only the activity of SEQ ID NO: 4 is necessary and according to the definition of homology in the instant specification (page 21) a sequence that is 70% or greater would be homologous and share a common evolutionary origin, thus the activity is an inherent property. Therefore, the limitations of the claims are met by this reference.

### ***Conclusion***

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10. No claims are allowable, however, claims 70-72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS *HR*  
Patent Examiner *9/30/04*